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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/893,080	12/19/1997	ALAN M. WARSHAWSKY		7559
5487	7590	03/03/2004	EXAMINER	
ROSS J. OEHLER AVENTIS PHARMACEUTICALS INC. ROUTE 202-206 MAIL CODE: D303A BRIDGEWATER, NJ 08807			KIFLE, BRUCK	
			ART UNIT	PAPER NUMBER
			1624	
DATE MAILED: 03/03/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

08/893,080

**Applicant(s)**

WARSHAWSKY ET AL.

**Examiner**

Bruck Kifle, Ph.D.

**Art Unit**

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 19 December 1997.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-47 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-47 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>9/11/97 and 9/08/9</u> . | 6) <input type="checkbox"/> Other: _____  |

***Claim Rejections - 35 USC § 112***

Claims 1-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The group defined as “C<sub>3</sub>-C<sub>9</sub> heteroaryl” is indefinite. A heteroaryl necessarily requires the presence of a heteroatom and cannot be made of only carbon atoms. The term “heteroaryl” should be defined in terms of how many atoms are present, how many and what kind of heteroatoms are involved, what size ring is intended and how many rings are present.

Claims 36, 37, 41, 42 and 46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for treating the diseases embraced by these claims.

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: The method of use claims are drawn in part to inhibiting MMP, treating a neoplastic disease, treating a cardiovascular disorder and treating MS

2) The state of the prior art: There are no known compounds of similar structure which have been demonstrated to treat any and all neoplastic diseases or cardiovascular diseases or MS.

No compound has ever been found that can treat a neoplastic disease generally even though massive efforts have been directed towards this end. Since this assertion is contrary to what is

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known in oncology, proof must be provided that this revolutionary assertion has merits. Nearly all anti neoplastic drugs are effective against only a limited group of related cancers. Therefore, a compound effective against a neoplastic disease generally would be a revolutionary exception. Applicant is asserting that he succeeded where others have failed. Where extensive efforts have all failed, it is reasonable for the Patent and Trademark Office to require proof that the claimed invention actually works for this specific utility. It is well established that a utility rejection is proper when scope of enablement is not reasonably correlated to the scope of the claims. (In re Vaeck 20 USPQ2d 1439, 1444, In re Ferens 163 USPQ 609).

In re Buting 163 USPQ 689 establishes that even clinical tests showing that a compound found to be useful in the treatment of two types of cancers was not sufficient for a much broader range.

Regarding claim 36, one skilled in the art cannot say for sure which patient is in need of inhibition of MMP. Is extensive experimentation required on the part of a potential infringer to determine if his use of Applicants' inhibitor falls within the limitations of applicants' claim? *In re Kirk and Petrow*, 153 USPQ 48 (CCPA 1967). As the Supreme Court said in *Brenner v. Manson*, 148 USPQ at 696: "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." As U.S. Court of Customs and Patent Appeals stated *In re Diedrich* 138 USPQ at 130, quoting with approval from the decision of the board: "We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his

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competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.”

“Cardiovascular disorders” embraces disorders which are opposites and that have very little in common. MS is known to be treated using interferon and is the only established therapy for multiple sclerosis. MMP inhibitors are not presently art-recognized to be efficacious for this purpose. Thus, the skilled clinician would not know how to use them to treat MS with Applicants' compounds. Case law is clear on this point. In an unpredictable art, such as MS therapy, models may be used for enablement only if there is a well-established correlation between the assay and clinical efficacy.

3) The predictability or lack thereof in the art: Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, “the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved”. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: There are no doses present to direct one to treat protect a host with any and all of the disorders embraced by these claims.

6) The breadth of the claims: The claims are drawn to disorders that are not related and whose treatment using a single drug is unknown.

7) The quantity of experimentation need would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan for the many reasons stated above.

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Thus, factors such as “sufficient working examples”, “the level of skill in the art” and “predictability”, etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruck Kifle, Ph.D. whose telephone number is 571-272-0668. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Mukund J. Shah can be reached on 571-272-0674. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.



Bruck Kifle, Ph.D.  
Primary Examiner  
Art Unit 1624

BK  
February 26, 2004